WEST Search History

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DATE: Thursday, July 08, 2004

Hide?	Set Name	Query	Hit Count
		DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L9	L8 and 424/450.ccls.	39
☐	L8	liposome adj5 vitamin	106
☐	L7	liposome same (stem adj1 cell) same (encapsula$)	42
☐	L6	liposome adj5 (stem adj1 cell)	10
☐	L5	liposome same (stem adj1 cell)	839
☐	L4	L3 and (fibroblast adj1 growth)	16
☐	L3	liposome same (endothelial adj1 growth)	24
☐	L2	L1 and fgf	21
☐	L1	liposome same vegf	78

END OF SEARCH HISTORY

DOCUMENT-IDENTIFIER: US 5919459 A
TITLE: Compositions and methods for treating cancer and hyperproliferative disorders

CLAIMS:

15. A composition comprising,

(a) a vascular endothelial growth factor or immunogenic peptide thereof; and

(b) a liposome wherein the vascular endothelial growth factor or immunogenic peptide thereof is incorporated into the liposome such that the composition is immunogenic for the vascular endothelial growth factor or immunogenic peptide thereof when administered to a human or animal.

22. A method of treating an individual in need of an immune response to a growth factor comprising administering to a human or animal an effective amount of an immunogenic vascular endothelial growth factor composition, wherein the composition comprises,

(a) a vascular endothelial growth factor or a peptide epitope thereof; and

(b) a liposome wherein the vascular endothelial growth factor or immunogenic peptide thereof is incorporated into the liposome such that the composition is immunogenic for the vascular endothelial growth factor or immunogenic peptide thereof when administered to a human or animal.

32. The composition of claim 15 wherein the vascular endothelial growth factor is conjugated to the liposome.

33. The composition of claim 15 wherein the vascular endothelial growth factor is encapsulated within the liposome.

34. The method of claim 22 wherein the vascular endothelial growth factor is conjugated to the liposome.

35. The method of claim 22 wherein the vascular endothelial growth factor is encapsulated within the liposome.

L9: Entry 22 of 39 File: USPT Jun 10, 1997

DOCUMENT-IDENTIFIER: US 5637315 A
TITLE: Treatment of disease states induced by oxidative stress

Drawing Description Text (5):
FIG. 4 illustrates a dose dependent curve which demonstrates that liposomes alone do not significantly inhibit the liver injury induced by carbon tetrachloride, but that liposomes containing increasing amounts of Vitamin E do inhibit the sublethal injury.

Drawing Description Text (6):
FIG. 5 illustrates that liposomes containing vitamin E markedly reduce the effects of a lethal dose of carbon tetrachloride.

Detailed Description Text (15):
Liposomes containing free radical scavengers, such as vitamin E, could be employed in the preservation of donor livers for transplantation. Prior to the harvesting of the liver, for example, about two hours prior to harvesting, at least one free radical scavenger or antioxidant and a liposome carrier could be given by normal intravenous infusion. Those skilled in the art recognize methods for determining the amount of free radical scavenger and/or antioxidant necessary to provide protective action lasting for the entire time between harvesting and implantation into the recipient. Moreover, the constituents of the liposome would also act as hepatoprotective agents during the operation and in the immediate postoperative period.

Detailed Description Text (25):
CF-1 mice (at least 3 per group) were injected intravenously with a preparation which combined a liposome with vitamin E, butylated hydroxytoluene, or ascorbic acid 6-palmitate or vitamin E succinate. Total lipid was 11.3 mg.

Detailed Description Text (28):
As shown in FIG. 3, vitamin E was much more efficient in reducing hepatic injury, as measured by a reduction in ALT (ALT=SGPT). These, and other similar experiments suggest that the preferred oxygen radical scavenger composition of the liposomes is vitamin E alone.

Detailed Description Text (30):
Liposomes were prepared as described for Example 2. In this experiment, one group of animals was injected with liposomes without vitamin E, while two others groups were injected with liposomes containing increasing amounts of vitamin E. All groups were then treated intraperitoneally with carbon tetrachloride. The vitamin E-treated mice had much less injury as measured by ALT levels.

Detailed Description Text (32):
Liposomes were prepared as described for Example 2. In this experiment, the first group (8 mice) received a lethal dose of carbon tetrachloride without any liposome therapy. All the animals died. The second group (8 mice) received liposomes containing vitamin E, and then two hours later received the lethal dose of carbon tetrachloride. Only one of the eight died in the treated group.

Current US Original Classification (1):
424/450

Other Reference Publication (3):
Motoyama, T. et al., "Synergistic Inhibition of Oxidation in Dispersed Phosphatidylcholine Liposomes by a Combination of Vitamin E and Cysteine", Archives of Biochemistry and Biopohysics 1989, 270(2), 655-661.

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DATE: Thursday, July 08, 2004

Hide?	Set Name	Query	Hit Count
	DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L2	L1 and 424/450.ccls.	96
☐	L1	liposome same (bone adj1 marrow)	357

END OF SEARCH HISTORY

L2: Entry 23 of 96 File: USPT Aug 29, 2000

DOCUMENT-IDENTIFIER: US 6110490 A
TITLE: Liposomal delivery system for biologically active agents

Detailed Description Text (28):
Alternatively, tissue targeting may be obtained by anchoring antibodies or ligands at the surface of the liposomes. Cell specificity of such liposome mediated delivery may be of particular importance in targeting cancer cells and bone marrow stem cells.

Detailed Description Text (38):
Using the DLS-liposome system, the human MDR1 gene is introduced into bone marrow cells ("BMC"). The transferred human MDR1 is expressed, as detected by staining with P-gp specific MRK16 monoclonal antibody, in all of the in vitro transfected BMC. Moreover, P-gp is detected in BMC from all transplanted animals tested, and from almost all of the in vivo treated animals.

Detailed Description Text (40):
The potential for obtaining drug resistant bone marrow progenitor cells after gene transfer using the instant liposome delivery system make it possible to protect cancer patients undergoing chemotherapy from marrow toxicity of anti-cancer drugs. In addition, the multidrug resistance gene serves as a positive selectable gene marker in vivo for insuring the expression of a non-selectable gene.

Detailed Description Text (43):
The development of the present liposome delivery system comprising DLS liposomes may be encapsulate episomal expression vectors so as to result in a broad biodistribution and persistence of transgene expression following a single intravenous ("i.v.") injection of liposomal DNA. The efficacy of DLS-liposomes used for the "in vivo" expression of the human MDR-1 gene is also disclosed in bone marrow progenitor cells by employing two different approaches: 1) a systemic delivery, and 2) an "ex vivo" approach by transplanting "in vitro" transfected BMC.

Detailed Description Text (95):
The MDR-1 gene expresses the P-glycoprotein ("P-gp"), a plasma membrane protein involved in the emergence of the Multi-drug Resistance phenotype which may occur after chemotherapy. The MDR-1 gene was used in this example as a marker of gene delivery in order to assess the efficacy of bone marrow transplant of MDR-1 gene transfected bone marrow cells by DLS-liposomes, both DLS-1 and DLS-2.

Detailed Description Text (96):
In order to assess the efficacy of bone marrow transplantation for "ex vivo" gene therapy, murine bone marrow cells were transfected with this plasmid and the DLS-liposomes and transplanted into Balb-C mice. The proliferation and differentiation of transduced hematopoietic progenitor cells were detected up to 21 days after transplantation in the spleen and the bone marrow, suggesting that the bone marrow transplant had taken place.

Detailed Description Text (97):
Murine bone marrow cells were harvested and quickly transfected with the pHaMDR GA

plasmid encapsulated in DLS-liposomes. Seven different experiments have confirmed that the MDR-1 gene was expressed in bone marrow cells since cells continue to grow under selective pressures (vincristine). In addition, lymphocyte, macrophage and fibroblast populations have been shown to exhibit the MDR phenotype after selection (using the rhodamine drug efflux method).

Detailed Description Text (100):
In order to achieve efficient liposomal transfection, both ex vivo and in vivo approaches have been used. The protocols shown in FIG. 1 were utilized. In examples 10-13, DLS-liposomes-2 are used. 1) the in vitro/ex vivo approach, in which mice were pre-treated with 5-fluoro Uracil ("5-FU") (150 mg/kg) by the method described in Hodgson et al. (1979 Nature 281:381-2) were sacrificed, and their bone marrow cells ("BMC") were transfected with 10 .mu.g of DLS/MDR in T25 culture flasks (Costar). BMC transfected with DLS/Neo was used as negative controls. After 4-5 days, BMC were transplanted into lethally irradiated mice. Some BMC were kept for analysis by FACSort, PCR or kept in suspension culture with or without vincristine for 48 hours after which they were tested in semisolid medium for their potency to form colonies. 2) The direct in vivo gene delivery approach was used, in which 2-3 days after being pre-treatment with 5-FU (150 mg/kg), mice were injected intravenously with 75 .mu.g DLS/MDR. All negative control mice were injected with DLS/Neo.

Detailed Description Text (147):
liposomes encapsulated plasmid at various DNA/lipid ratios were assayed. In these experiments transgene expression has been assayed in liver, lung and spleen. Luciferase activity was determined by bioluminescence measurement (2-3 mice/point). More than 100 mice have been studied. PCR analysis showed the long lasting expression of the lucriferase gene in all tissues tested (lung, liver, heart, spleen, skeletal muscle, blood cells, bone marrow, and ovary) up to at least 2 months post-injection. Only episomal replicating DNA vectors showed positive results.

Current US Original Classification (1):
424/450

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L2: Entry 11 of 96 File: USPT Jul 30, 2002

DOCUMENT-IDENTIFIER: US 6426086 B1
TITLE: pH-sensitive, serum-stable liposomes

Detailed Description Text (28):
Liposomes of the invention can be used in vitro for a variety of purposes. For examples, liposomes can be used to carry into cultured cells drugs or other agents which are otherwise difficult to get through biological membranes. Such agents can include large molecular weight compounds, compounds which would be affected by plasma proteases, nucleases, or other enzymes, and compounds which would otherwise not be readily transported across the cell membrane. In one preferred embodiment, the liposomes bear ligands overexpressed by cancer cells and contain a cytotoxic agent. In this embodiment, the liposomes preferentially bind to any cancer cells in the cultured population, are internalized, and kill the cancer cells. Thus, the liposomes of the invention can be used to purge a cultured cell population of any cancer cells bearing a marker which distinguishes those cells from the general cell population. If desired, the cells remaining after the cancer cells have been eliminated or reduced in number can be infused into a patient in need thereof. For example, bone marrow cells taken from a patient can be purged of cancer cells ex vivo and the remaining cells can be reinfused into the patient. The Examples demonstrate the delivery of a widely-used anticancer agent, doxirubicin, to human cancer cells.

Current US Original Classification (1):
424/450

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DATE: Thursday, July 08, 2004

Hide?	Set Name	Query	Hit Count
	DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L11	L10 and cholesterol	58
☐	L10	(liposome) same (dioleoylphosphatidylethanolamine) same (dipalmitoylphosphatidylcholine)	59
☐	L9	L6 and (7 adj1 micron)	11
☐	L8	L6 and giant	0
☐	L7	L6 giant	12604
☐	L6	L5 and cholesterol	70
☐	L5	L3 and dipalmitoylphosphatidylcholine	72
☐	L4	L3 and dipamitoylphosphatidylcholine	0
☐	L3	(liposome) same (dioleoylphosphatidylethanolamine)	239
☐	L2	L1 and dioleoyl$	5
☐	L1	(giant adj3 liposome)	32

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DATE: Thursday, July 08, 2004

Hide?	Set Name	Query	Hit Count
		DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L9	L6 and (7 adj1 micron)	11
☐	L8	L6 and giant	0
☐	L7	L6 giant	12604
☐	L6	L5 and cholesterol	70
☐	L5	L3 and dipalmitoylphosphatidylcholine	72
☐	L4	L3 and dipamitoylphosphatidylcholine	0
☐	L3	(liposome) same (dioleoylphosphatidylethanolamine)	239
☐	L2	L1 and dioleoyl$	5
☐	L1	(giant adj3 liposome)	32

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L2: Entry 2 of 5 File: USPT Dec 8, 1998

DOCUMENT-IDENTIFIER: US 5846951 A
** See image for Certificate of Correction **
TITLE: Pharmaceutical compositions

Other Reference Publication (1):
Biochemica et Biophysica Acta, vol. 986, 1989, Amsterdam, NL, pp. 106-114, Abstract Pinnaduwge et al `The Role of Protein-Linked Oligosaccharide in the Bilayer Staliziation Activity of Glycophorin A For Dioleoylphosphatidylethanolamine Liposomes`.

Other Reference Publication (2):
Biochemica et Biophysica Acta, vol. 1023, 1990, Amsterdam, NL, pp. 357-364, Abstract Decher et al `Giant Liposomes as Model Membranes for Immunological Studies: Spontaneous Insertion of Purified K1-Antigen (Poly-Alpha-2,8-Neuac) of Escherichia Coli`.

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L2: Entry 4 of 5 File: USPT Apr 25, 1995

DOCUMENT-IDENTIFIER: US 5409704 A
TITLE: Liposomes comprising aminoglycoside phosphates and methods of production and use

Detailed Description Text (13):
The second broad class of lipid materials used in this invention are amphipathic in character. Hydrophilic character could be imparted to the molecule through the presence of phosphato, carboxylic, sulphato, amino, sulfhydryl, nitro, and other like groups. Hydrophobicity could be conferred by the inclusion of groups that include, but are not limited to, long chain saturated and unsaturated aliphatic hydrocarbon groups and such groups substituted by one or more aromatic, cycloaliphatic or heterocyclic group. The preferred amphipathic compounds are phosphoglycerides, representative examples of which include phosphatidylcholine, phosphatidylethanolamine, lysophosphatidylcholine, lysophosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidic acid, dimyristoylphosphatidylglycerol and diphosphatidylglycerol alone or in combination with other lipids. Synthetic saturated compounds such as dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine, or distearoylphosphatidylcholine or unsaturated species such as dioleoylphosphatidylcholine or dilinoleoylphosphatidylcholine might also be usable. Other compounds lacking phosphorous, such as members of the sphingolipid and glycosphingolipid families, are also within the group designated as lipid.

Other Reference Publication (52):
Oku, et al., "Differential Effects of Alkali Metal Chlorides on Formation of Giant Liposomes by Freezing and Thawing and Dialysis", Biochem, 1983, 22(4):855-863.

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L2: Entry 5 of 5 File: USPT Aug 29, 1989

DOCUMENT-IDENTIFIER: US 4861597 A
TITLE: Novel functionallized liposomes and a process for production thereof

Detailed Description Text (6):
As constitutive materials for the liposomes of this invention, there can be used all the constitutive material usually used in known methods for producing liposomes, for example, phospholipids such as natural lecithins (e.g., egg yolk lecithin, soybean lecithin, etc.), dipalmitoyl phosphatidyl choline (DPPC), dimyristoyl phosphatidyl choline (DMPC), distearoyl phosphatidyl choline (DSPC), dioleoyl phosphatidyl choline (DOPC), dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl glycerol (DPPG), dimyristoyl phosphatidic acid (DMPA), and the like alone or in combination of two or more thereof, and mixtures thereof with cholesterols, etc.

Detailed Description Text (10):
As a method for producing the liposomes of this invention, there may be exemplified all the per se well-known methods for producing liposomes, for example, heretofore well known methods such as the vortexing method, sonication method, surfactant method, reverse-phase evaporation method (REV method), ethanol infusion method, ether infusion method, pre-vesical method, French press extrusion method, Ca.sup.2+ fusion method, annealing method, freeze-thaw-fusion method, W/O/W emulsion method, etc.; methods such as the stable plurilamellar vesicle method (SPLV method) recently reported by S. M. Gruner et al. (Biochemistry, 24, 2833 (1985)); and methods for preparing liposomes called "giant liposomes" which have a large captured volume.

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Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: US 6358523 B1

Using default format because multiple data bases are involved.

L2: Entry 1 of 5 File: USPT Mar 19, 2002

US-PAT-NO: 6358523
DOCUMENT-IDENTIFIER: US 6358523 B1

TITLE: Macromolecule-lipid complexes and methods for making and regulating

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Safinya; Cyrus R.	Santa Barbara	CA		
Raedler; Joachim Oskar	Garching			DE
Koltover; Ilya	Pasadena	CA		

US-CL-CURRENT: 424/450; 424/400, 424/405, 424/484, 424/9.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 5846951 A

L2: Entry 2 of 5 File: USPT Dec 8, 1998

US-PAT-NO: 5846951
DOCUMENT-IDENTIFIER: US 5846951 A
**** See image for Certificate of Correction ****

TITLE: Pharmaceutical compositions

DATE-ISSUED: December 8, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gregoriadis; Gregory	Middlesex			GB

US-CL-CURRENT: 514/54; 424/450, 424/461, 514/42

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 5419914 A

L2: Entry 3 of 5 File: USPT May 30, 1995

US-PAT-NO: 5419914
DOCUMENT-IDENTIFIER: US 5419914 A

TITLE: Phospholipid analogue vesicle

DATE-ISSUED: May 30, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sullivan; Sean M.	Pasadena	CA		

US-CL-CURRENT: 424/450; 428/402.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 4. Document ID: US 5409704 A

L2: Entry 4 of 5 File: USPT Apr 25, 1995

US-PAT-NO: 5409704
DOCUMENT-IDENTIFIER: US 5409704 A

TITLE: Liposomes comprising aminoglycoside phosphates and methods of production and use

DATE-ISSUED: April 25, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bally; Marcel B.	Vancouver			CA
Bolcsak; Lois E.	Lawrenceville	NJ		
Cullis; Pieter R.	Vancouver			CA
Janoff; Andrew S.	Yardley	PA		
Mayer; Lawrence D.	Vancouver			CA

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 428/402.2, 514/37, 514/78, 514/912, 514/913, 514/914

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 5. Document ID: US 4861597 A

L2: Entry 5 of 5 File: USPT Aug 29, 1989

US-PAT-NO: 4861597
DOCUMENT-IDENTIFIER: US 4861597 A

TITLE: Novel functionallized liposomes and a process for production thereof

DATE-ISSUED: August 29, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kida; Masaaki	Suita			JP
Kitabata; Isako	Amagasaki			JP
Kubotsu; Kazuhisa	Osaka			JP
Sakata; Yoshitsugu	Otsu			JP

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.32, 264/4.33, 424/178.1, 424/812, 428/402.21, 428/402.24

Terms	Documents
L1 and dioleoyl$	5

L9: Entry 10 of 11 File: USPT Aug 6, 1996

DOCUMENT-IDENTIFIER: US 5542935 A
** See image for Certificate of Correction **
TITLE: Therapeutic delivery systems related applications

Brief Summary Text (12):
Ryan et al., in U.S. Pat. No. 4,544,545, disclose phospholipid liposomes having a chemically modified cholesterol coating. The cholesterol coating may be a monolayer or bilayer. An aqueous medium, containing a tracer, therapeutic, or cytotoxic agent, is confined within the liposome. Liposomes, having a diameter of 0.001 microns to 10 microns, are prepared by agitation and ultrasonic vibration.

Brief Summary Text (23):
Despite the advances that have been made, the prior art has still not solved many of the problems inherent in the development of ultrasound contrast agents. Gases may diffuse out of stabilizing emulsions or particle coatings and the efficacy of the product may be lost. In all of the gaseous based contrast media for ultrasound under development to date, the microspheres are relatively large, e.g. on the order of 2 to 7 microns, such that sufficient backscatter for ultrasonic contrast enhancement is provided. The large size of these particles makes it very difficult to exclude potential contaminants from the injection such as bacteria passing into the patient during the injection. Gas-containing microspheres currently under development are generally unstable in vivo and do not persist long enough to provide ideal contrast enhancement.

Detailed Description Text (11):
Similarly, perfluoropentane which is liquid at room temperature may be entrapped in liposomes. A small quantity (0.76-1.52 .mu.L) of the liquid perfluoropentane precursor may be added to a lipid solution (e.g. 82 mole % dipalmitoylphosphatidylcholine, 8 mole % dipalmitoylphosphatidylethanolamine-PEG 500 and 10 mole % dipalmitoylphosphatidic acid) in a solution of 80 volume % normal saline, 10 volume % glycerol with 10 volume % propylene glycol at room temperature and shaken. Then the temperature of the suspension is raised past the phase transition temperature (e.g. over 30.degree. C.) to initiate the liquid to gaseous conversion of the perfluoropentane gaseous precursor. Foaming results and gas filled liposomes are produced. The mean size of gas filled liposomes produced are generally in excess of 20 microns as produced by vortexing or shaking on a Wig-L-Bug.TM.. The liposomes can be filtered and a single passage through an 8.0 micron filter is adequate to remove more than 99% of the particles over 10 microns in size. As the liposomes are compliant and pliable, they reform into smaller lipid coated liposomes after filtration. When the liposomes are cooled to room temperature or lower, the entrapped perfluoropentane gaseous precursor goes back into the liquid state and the result is entrapped nanodroplets of perfluoropentane within the liposomes. Upon rewarming (e.g. injection in vivo) the appropriate sized gas liposomes then form.

Detailed Description Text (13):
A micellular formulation may be substituted for a liposome (lipid bilayers entrapping the nanodroplet of perfluoropentane). A micellular formulation has the appropriate mixture of lipids, e.g. peanut oil with sodium cholate, cholesterol and glycerol (optionally with a portion of PEGylated lipids). A microfluidizer process

can be used to produce a micellular formulation of the gaseous precursor to produce nanoparticles or microparticles of the emulsion wherein each particle entraps on average a nanodroplet of about 5 nm diameter or less of perfluoropentane.

Detailed Description Text (65):
Freeze drying is useful to remove water and organic materials from the lipids prior to the shaking gas instillation method. Drying-gas instillation method may be used to remove water from liposomes. By pre-entrapping the gaseous precursor in the dried liposomes (i.e. prior to drying) after warming, the gaseous precursor may expand to fill the liposome. Gaseous precursors can also be used to fill dried liposomes after they have been subjected to vacuum. As the dried liposomes are kept at a temperature below their gel state to liquid crystalline temperature the drying chamber can be slowly filled with the gaseous precursor in its gaseous state, e.g. perfluorobutane can be used to fill dried liposomes composed of dipalmitoylphosphatidylcholine (DPPC) at temperatures between 3.degree. C. (the boiling point of perfluorobutane) and below 40.degree. C., the phase transition temperature of the lipid. In this case, it would be most preferred to fill the liposomes at a temperature about 4.degree. C. to about 5.degree. C.

Detailed Description Text (82):
In addition, it has been found that the gaseous precursor-filled liposomes of the present invention can be stabilized with lipids covalently linked to polymers of polyethylene glycol, commonly referred to as PEGylated lipids. It has also been found that the incorporation of at least a small amount of negatively charged lipid, or a lipid having a net negative charge, into any liposome membrane, although not required, is beneficial to providing liposomes that do not have a propensity to rupture by fusing together. By at least a small amount, it is meant about 1 to about 10 mole percent of the total lipid. Suitable negatively charged lipids will be readily apparent to those skilled in the art, and include, for example, phosphatidylserine and fatty acids. Most preferred for ability to rupture on application of resonant frequency ultrasound, echogenicity and stability are liposomes prepared from dipalmitoylphosphatidylcholine.

Detailed Description Text (92):
Lipids which may be used to create liposome microspheres include but are not limited to: lipids such as fatty acids, lysolipids, phosphatidylcholine with both saturated and unsaturated lipids including dioleoylphosphatidylcholine; dimyristoylphosphatidylcholine; dipentadecanoylphosphatidylcholine, dilauroylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine; distearoylphosphatidylcholine; phosphatidylethanolamines such as dioleoylphosphatidylethanolamine; phosphatidylserine; phosphatidylglycerol; phosphatidylinositol, sphingolipids such as sphingomyelin; glycolipids such as ganglioside GM1 and GM2; glucolipids; sulfatides; glycosphingolipids; phosphatidic acid; palmitic acid; stearic acid; arachidonic acid; oleic acid; lipids bearing polymers such as polyethyleneglycol, chitin, hyaluronic acid or polyvinylpyrrolidone; lipids bearing sulfonated mono-, di-, oligo- or polysaccharides; cholesterol, cholesterol sulfate and cholesterol hemisuccinate; tocopherol hemisuccinate, lipids with ether and ester-linked fatty acids, polymerized lipids, diacetyl phosphate, stearylamine, cardiolipin, phospholipids with short chain fatty acids of 6-8 carbons in length, synthetic phospholipids with asymmetric acyl chains (e.g., with one acyl chain of 6 carbons and another acyl chain of 12 carbons), 6-(5-cholesten-3.beta.-yloxy)-1-thio-.beta.-D-galactopyranoside, digalactosyldiglyceride, 6-(5-cholesten-3.beta.-yloxy)hexyl-6-amino-6-deoxy-1-thio-.beta.-D-galacto pyranoside, 6-(5-cholesten-3.beta.-yloxy) hexyl-6-amino-6-deoxyl-1-thio-.alpha.-D-mannopyranoside, 12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)-octadecanoic acid; N-[12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methyl-amino) octadecanoyl]-2-aminopalmitic acid; cholesteryl)4'-trimethyl-ammonio)butanoate; N-succinyldioleoylphosphatidylethanolamine; 1,2-dioleoyl-sn-glycerol;1,2-dipalmitoyl-sn-3-succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol;1-hexadecyl-2-

palmitoylglycerophosphoet hanolamine and palmitoylhomocysteine, and/or combinations thereof. The liposomes may be formed as monolayers or bilayers and may or may not have a coating.

Detailed Description Text (95):
If desired, either anionic or cationic lipids may be used to bind anionic or cationic pharmaceuticals. Cationic lipids may be used to bind DNA and RNA analogues with in or on the surface of the gaseous precursor-filled microsphere. A variety of cationic lipids such as DOTMA, N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammoium chloride; DOTAP, 1,2-dioleoyloxy-3-(trimethylammonio)propane; and DOTB, 1,2-dioleoyl-3-(4'-trimethyl-ammonio)butanoyl-sn-glycerol may be used. In general the molar ratio of cationic lipid to non-cationic lipid in the liposome may be, for example, 1:1000, 1:100, preferably, between 2:1 to 1:10, more preferably in the range between 1:1 to 1:2.5 and most preferably 1:1 (ratio of mole amount cationic lipid to mole amount non-cationic lipid, e.g., DPPC). A wide variety of lipids may comprise the non-cationic lipid when cationic lipid is used to construct the microsphere. Preferably, this non-cationic lipid is dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylethanolamine or dioleoylphosphatidylethanolamine. In lieu of cationic lipids as described above, lipids bearing cationic polymers such as polylysine or polyarginine may also be used to construct the microspheres and afford binding of a negatively charged therapeutic, such as genetic material, to the outside of the microspheres. As an example, anionic lipids may consist of but are by no means limited to sodium dodecyl sulfate, steraric acid, palmitic acid, phosphatidic acid, and cholesterol sulfate.

Detailed Description Text (101):
Emulsifying and/or solubilizing agents may also be used in conjunction with lipids or liposomes. Such agents include, but are not limited to, acacia, cholesterol, diethanolamine, glyceryl monostearate, lanolin alcohols, lecithin, mono- and di-glycerides, mono-ethanolamine, oleic acid, oleyl alcohol, poloxamer, peanut oil, palmitic acid, polyoxyethylene 50 stearate, polyoxyl 35 castor oil, polyoxyl 10 oleyl ether, polyoxyl 20 cetostearyl ether, polyoxyl 40 stearate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, propylene glycol diacetate, propylene glycol monostearate, sodium lauryl sulfate, sodium stearate, sorbitan mono-laurate, sorbitan mono-oleate, sorbitan mono-palmitate, sorbitan monostearate, stearic acid, trolamine, and emulsifying wax. All lipids with perfluoro fatty acids as a component of the lipid in lieu of the saturated or unsaturated hydrocarbon fatty acids found in lipids of plant or animal origin may be used. Suspending and/or viscosity-increasing agents that may be used with lipid or liposome solutions include, but are not limited to, acacia, agar, alginic acid, aluminum mono-stearate, bentonite, magma, carbomer 934P, carboxymethylcellulose, calcium and sodium and sodium 12, carrageenan, cellulose, dextrin, gelatin, guar gum, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium aluminum silicate, methylcellulose, pectin, polyethylene oxide, polyvinyl alcohol, povidone, propylene glycol alginate, silicon dioxide, sodium alginate, tragacanth, and xanthum gum.

Detailed Description Text (113):
Prodrugs may also be designed as reversible drug derivatives and utilized as modifiers to enhance drug transport to site-specific tissues. Examples of parent molecules with reversible modifications or linkages to influence transport to a site specific tissue and for enhanced therapeutic effect include isocyanate with haloalkyl nitrosurea, testosterone with propionate ester, methotrexate (3-5'-dichloromethotrexate) with dialkyl esters, cytosine arabinoside with 5'-acylate, nitrogen mustard (2,2'-dichloro-N-methyldiethylamine), nitrogen mustard with aminomethyl tetracycline, nitrogen mustard with cholesterol or estradiol or dehydroepiandrosterone esters and nitrogen mustard with azobenzene.

Detailed Description Text (201):
Filtration is preferably carried out in order to obtain gaseous precursor-filled liposomes of a substantially uniform size. In certain preferred embodiments, the

filtration assembly contains more than one filter, and preferably, the filters are not immediately adjacent to each other, as illustrated in FIG. 12. Before filtration, the gaseous precursor-filled liposomes range in size from about 1 micron to greater than 60 microns (FIGS. 15A and 16A). After filtration through a single filter, the gaseous precursor-filled liposomes are generally less than 10 microns but particles as large as 25 microns in size remain. After filtration through two filters (10 micron followed by 8 micron filter), almost all of the liposomes are less than 10 microns, and most are 5 to 7 microns (FIGS. 15B and 16B).

Detailed Description Text (226):
To prepare the therapeutic containing liposomes for vacuum drying gas installation, and by way of general guidance, dipalmitoylphosphatidylcholine liposomes, for example, may be prepared by suspending dipalmitoylphosphatidylcholine lipids in phosphate buffered saline or water containing the therapeutic to be encapsulated, and heating the lipids to about 50.degree. C., a temperature which is slightly above the 41.degree. C. temperature required for transition of the dipalmitoylphosphatidylcholine lipids from a gel state to a liquid crystalline state, to form therapeutic containing liposomes.

Detailed Description Text (227):
To prepare multilamellar vesicles of a rather heterogeneous size distribution of around 2 microns, the liposomes may then be mixed gently by hand while keeping the liposome solution at a temperature of about 50.degree. C. The temperature is then lowered to room temperature, and the liposomes remain intact. Extrusion of dipalmitoylphosphatidylcholine liposomes through polycarbonate filters of defined size may, if desired, be employed to make liposomes of a more homogeneous size distribution. A device useful for this technique is an extruder device (Extruder Device.TM., Lipex Biomembranes, Vancouver, Canada) equipped with a thermal barrel so that extrusion may be conveniently accomplished above the gel state to liquid crystalline state phase transition temperature for lipids.

Detailed Description Text (228):
For lipophilic therapeutics which are sparingly soluble in aqueous media, such therapeutics may be mixed with the lipids themselves prior to forming the liposomes. For example, amphotericin may be suspended with the dried lipids (e.g., 8:2 molar ratio of egg phosphatidylcholine and cholesterol in chloroform and mixed with the lipids). The chloroform is then evaporated (note that other suitable organic solvents may also be used, such as ethanol or ether) and the dried lipids containing a mixture of the lipophilic therapeutics are then resuspended in aqueous media, e.g., sterile water or physiologic saline. This process may be used for a variety of lipophilic therapeutics such as corticosteroids to incorporate lipophilic drugs into the liposome membranes. The resulting liposomes are then dried, subjected to the vacuum gas instillation method as described above.

Detailed Description Text (229):
Alternatively, and again by way of general guidance, conventional freeze-thaw procedures may be used to produce either oligolamellar or unilamellar dipalmitoylphosphatidylcholine liposomes. After the freeze-thaw procedures, extrusion procedures as described above may then be performed on the liposomes.

Detailed Description Text (249):
Gas-filled liposomes were synthesized as follows: Pure dipalmitoylphosphatidylcholine (DPPC), Avanti Polar Lipids, Alabaster, Ala., was suspended in normal saline and then Extruded five times through 2 micron polycarbonate filters (Nuclepore, Costar, Pleasanton, Calif.) using an Extruder Device (Lipex Biomembranes, Vancouver, Canada) at 800 p.s.i. The resulting liposomes were then dried under reduced pressure as described in U.S. Ser. No. 716,899, filed Jun. 18, 1991, which is hereby incorporated by reference in its entirety. After thorough drying the dried liposomes were then slowly filled with

nitrogen gas, as described in U.S. Ser. No. 716,899. After equilibration with ambient pressure, the resulting liposomes were suspended in saline solution (0.9% NaCl) and shaken vigorously.

Detailed Description Text (292):
Dipalmitoylphosphatidylcholine (1 gram) is suspended in 10 ml phosphate buffered saline containing the drug adriamycin, the suspension is heated to about 50.degree. C., and then is swirled by hand in a round bottom flask for about 30 minutes. The heat source is removed, and the suspension is swirled for two additional hours, while allowing the suspension to cool to room temperature, to form drug containing liposomes.

Detailed Description Text (297):
Dipalmitoylphosphatidylcholine (1 gram) and the cryoprotectant trehalose (1 gram) are suspended in 10 ml phosphate buffered saline containing the drug amphotericin-B, the suspension is heated to about 50.degree. C., and then is swirled by hand in a round bottom flask for about 30 minutes. The heat source is removed, and the suspension is swirled for about two additional hours, while allowing the suspension to cool to room temperature, to form liposomes.

Detailed Description Text (302):
Dipalmitoylphosphatidylcholine (1 gram) is suspended in 10 ml phosphate buffered saline containing the drug cytosine arabinosine, the suspension is heated to about 50.degree. C., and then swirled by hand in a round bottom flask for about 30 minutes. The suspension is then subjected to 5 cycles of extrusion through an extruder device jacketed with a thermal barrel (Extruder Device.TM., Lipex Biomembranes, Vancouver, Canada), both with and without conventional freeze-thaw treatment prior to extrusion, while maintaining the temperature at about 50.degree. C. The heat source is removed, and the suspension is swirled for about two additional hours, while allowing the suspension to cool to room temperature, to form liposomes.

Detailed Description Text (342):
250 mg DPPC (dipalmitoylphosphatidylcholine) and 10 ml of 0.9% NaCl were added to a 50 ml Falcon centrifuge tube (Becton-Dickinson, Lincoln Park, N.J.) and maintained at an ambient temperature (approx. 20.degree. C.). The suspension was then extruded through a 1 .mu.m "NUCLEPORE" (Costar, Pleasanton, Calif.) polycarbonate membrane under nitrogen pressure. The resultant suspension was sized on a Particle Sizing Systems (Santa Barbara, Calif.) Model 370 laser light scattering sizer. All lipid particles were 1 .mu.m or smaller in mean outside diameter.

Detailed Description Text (350):
10 ml of a solution of 1,2-dipalmitoylphosphatidylcholine at 25mg/ml in 0.9% NaCl, which had previously been extruded through a 1 .mu.m filter and autoclaved for twenty minutes, was added to a Falcon 50 ml centrifuge tube (Becton-Dickinson, Lincoln Park, N.J.). After equilibration of the lipid suspension to room temperature (approximately 20.degree. C.), the liquid was vortexed on a VWR Genie-2 (120 V, 0.5 amp, 60 Hz.) (Scientific Industries, Inc., Bohemia, N.Y.) for 10 minutes or until a time that the total volume of gas-filled liposomes was at least double or triple the volume of the original aqueous lipid solution. The solution at the bottom of the tube was almost totally devoid of anhydrous particulate lipid, and a large volume of foam containing gas-filled liposomes resulted. Thus, prior autoclaving does not affect the ability of the lipid suspension to form gas-filled liposomes. Autoclaving does not change the size of the liposomes, and it does not decrease the ability of the lipid suspensions to form gas-filled liposomes.

Detailed Description Text (352):
10 ml of a solution of 1,2-dipalmitoylphosphatidylcholine at 25 mg/ml in 0.9% NaCl, which had previously been extruded through a 1 .mu.m filter and autoclaved for twenty minutes, was added to a Falcon 50 ml centrifuge tube (Becton-Dickinson,

Lincoln Park, N.J.). After equilibration of the lipid suspension to room temperature (approximately 20.degree. C.), the tube was then placed upright on a VWR Scientific Orbital shaker (VWR Scientific, Cerritos, Calif.) and shaken at 300 r.p.m. for 30 minutes. The resultant agitation on the shaker table resulted in the production of gas-filled liposomes.

Detailed Description Text (354):
10 ml of a solution of 1,2-dipalmitoylphosphatidylcholine at 25 mg/ml in 0.9% NaCl, which had previously been extruded through a 1 .mu.m filter and autoclaved for twenty minutes, was added to a Falcon 50 ml centrifuge tube (Becton-Dickinson, Lincoln Park, N.J.). After equilibration of the lipid suspension to room temperature (approximately 20.degree. C.), the tube was immobilized inside a 1 gallon empty household paint container and subsequently placed in a mechanical paint mixer employing a gyrating motion for 15 minutes. After vigorous mixing, the centrifuge tube was removed, and it was noted that gas-filled liposomes had formed.

Detailed Description Text (356):
10 ml of a solution of 1,2-dipalmitoylphosphatidylcholine at 25 mg/ml in 0.9% NaCl, which had previously been extruded through a 1 .mu.m nuclepore filter and autoclaved for twenty minutes, was added to a Falcon 50 ml centrifuge tube (Becton-Dickinson, Lincoln Park, N.J.). After equilibration of the lipid suspension to room temperature (approximately 20.degree. C.), the tube was shaken forcefully by hand for ten minutes. Upon ceasing agitation, gas-filled liposomes were formed.

Other Reference Publication (22):
Sankaram et al., "Cholesterol-induced fluid-phase immiscibility in membranes", Proc. Natl. Acad. Sci., 1991, 88:8686-8690.

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Search Results - Record(s) 1 through 11 of 11 returned.

☐ 1. Document ID: US 6479034 B1

Using default format because multiple data bases are involved.

L9: Entry 1 of 11 File: USPT Nov 12, 2002

US-PAT-NO: 6479034
DOCUMENT-IDENTIFIER: US 6479034 B1

TITLE: Method of preparing gas and gaseous precursor-filled microspheres

DATE-ISSUED: November 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 424/9.51; 424/450, 424/459, 424/9.5, 424/9.52

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 6443898 B1

L9: Entry 2 of 11 File: USPT Sep 3, 2002

US-PAT-NO: 6443898
DOCUMENT-IDENTIFIER: US 6443898 B1

TITLE: Therapeutic delivery systems

DATE-ISSUED: September 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		

Ramaswami; VaradaRajan	Tucson	AZ
Yellowhair; David	Tucson	AZ
Wu; Guanli	Tucson	AZ

US-CL-CURRENT: 600/458; 424/450, 424/9.51

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 3. Document ID: US 6071495 A

L9: Entry 3 of 11 File: USPT Jun 6, 2000

US-PAT-NO: 6071495
DOCUMENT-IDENTIFIER: US 6071495 A

TITLE: Targeted gas and gaseous precursor-filled liposomes

DATE-ISSUED: June 6, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 424/9.51; 424/450, 424/812, 424/9.52

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 4. Document ID: US 5935553 A

L9: Entry 4 of 11 File: USPT Aug 10, 1999

US-PAT-NO: 5935553
DOCUMENT-IDENTIFIER: US 5935553 A
**** See image for Certificate of Correction ****

TITLE: Methods of preparing gas-filled liposomes

DATE-ISSUED: August 10, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		

Ramaswami; VaradaRajan	Tucson	AZ
Yellowhair; David	Tucson	AZ
Wu; Guanli	Tucson	AZ

US-CL-CURRENT: 424/9.51; 424/450, 424/9.52, 600/458

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 5853752 A

L9: Entry 5 of 11 File: USPT Dec 29, 1998

US-PAT-NO: 5853752
DOCUMENT-IDENTIFIER: US 5853752 A
**** See image for Certificate of Correction ****

TITLE: Methods of preparing gas and gaseous precursor-filled microspheres

DATE-ISSUED: December 29, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 424/1.21, 424/489, 424/9.321, 424/9.51, 436/829

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 6. Document ID: US 5770222 A

L9: Entry 6 of 11 File: USPT Jun 23, 1998

US-PAT-NO: 5770222
DOCUMENT-IDENTIFIER: US 5770222 A

TITLE: Therapeutic drug delivery systems

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		

Matsunaga; Terry	Tucson	AZ
Ramaswami; VaradaRajan	Tucson	AZ
Yellowhair; David	Tucson	AZ
Wu; Guanli	Tucson	AZ

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 424/1.21, 424/489, 424/9.321, 424/9.51, 436/829

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 7. Document ID: US 5715824 A

L9: Entry 7 of 11 File: USPT Feb 10, 1998

US-PAT-NO: 5715824
DOCUMENT-IDENTIFIER: US 5715824 A
**** See image for Certificate of Correction ****

TITLE: Methods of preparing gas-filled liposomes

DATE-ISSUED: February 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 424/9.51; 264/4.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 8. Document ID: US 5585112 A

L9: Entry 8 of 11 File: USPT Dec 17, 1996

US-PAT-NO: 5585112
DOCUMENT-IDENTIFIER: US 5585112 A
**** See image for Certificate of Correction ****

TITLE: Method of preparing gas and gaseous precursor-filled microspheres

DATE-ISSUED: December 17, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		

Fritz; Thomas A.	Tucson	AZ
Matsunaga; Terry	Tucson	AZ
Ramaswami; VaradaRajan	Tucson	AZ
Yellowhair; David	Tucson	AZ
Wu; Guanli	Tucson	AZ

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 424/9.51

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 9. Document ID: US 5580575 A

L9: Entry 9 of 11 File: USPT Dec 3, 1996

US-PAT-NO: 5580575
DOCUMENT-IDENTIFIER: US 5580575 A
**** See image for Certificate of Correction ****

TITLE: Therapeutic drug delivery systems

DATE-ISSUED: December 3, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 424/450

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 10. Document ID: US 5542935 A

L9: Entry 10 of 11 File: USPT Aug 6, 1996

US-PAT-NO: 5542935
DOCUMENT-IDENTIFIER: US 5542935 A
**** See image for Certificate of Correction ****

TITLE: Therapeutic delivery systems related applications

DATE-ISSUED: August 6, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Unger; Evan C.	Tucson	AZ
Fritz; Thomas A.	Tucson	AZ
Matsunaga; Terry	Tucson	AZ
Ramaswami; VaradaRajan	Tucson	AZ
Yellowhair; David	Tucson	AZ
Wu; Guanli	Tucson	AZ

US-CL-CURRENT: 604/190; 424/450, 600/458

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 5469854 A

L9: Entry 11 of 11 File: USPT Nov 28, 1995

US-PAT-NO: 5469854
DOCUMENT-IDENTIFIER: US 5469854 A
**** See image for Certificate of Correction ****

TITLE: Methods of preparing gas-filled liposomes

DATE-ISSUED: November 28, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Fritz; Thomas A.	Tucson	AZ		
Matsunaga; Terry	Tucson	AZ		
Ramaswami; VaradaRajan	Tucson	AZ		
Yellowhair; David	Tucson	AZ		
Wu; Guanli	Tucson	AZ		

US-CL-CURRENT: 600/458; 264/4.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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L11: Entry 45 of 58 File: USPT Sep 9, 1997

DOCUMENT-IDENTIFIER: US 5665381 A
TITLE: Inhibition of aggregation of drug containing particles

Brief Summary Text (6):
The result is a spherical bilayer membrane in which the fatty acid tails point towards the interior of the membrane, and the polar heads point toward the aqueous medium. The polar heads at the inner surface of the membrane point toward the liposome's aqueous interior and those at the other (outer) surface point toward the exterior aqueous medium (i.e., the external continuous phase of the liposome dispersion). Liposomes may be either multilamellar, like an onion, with liquid separating many lipid bilayers, or unilamellar, with a single bilayer surrounding a liquid center. Finely divided phospholipids dispersed in aqueous solution spontaneously form bilayers, and simple agitation of the mixture usually produces multilamellar vesicles (MLVs), structures having diameters of 1-10 .mu.m (1000-10,000 nm). Sonication of these structures, or other methods known in the art, leads to formation of unilamellar vesicles (UVs) having an average diameter of about 30-200 nm. The actual equilibrium diameter is largely determined by the nature of the phospholipid used, the suspending buffer, and the extent of incorporation of other lipids such as cholesterol. Standard methods for the formation of liposomes are known in the art, for example, methods for the commercial production of liposomes are described in U.S. Pat. No. 4,753,788 to Ronald C. Gamble and U.S. Pat. No. 4,935,171 to Kevin R. Bracken, the disclosures of which are incorporated herein by reference.

Brief Summary Text (19):
Such liposome bilayer membrane particles include ones made from dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, dioleoylphosphatidylethanolamine, distearoylphosphatidylserine, dilinoleoylphosphatidylinositol, distearoylphosphatidylglycerol, and the like, or mixtures thereof. Liposome bilayer membrane particles made entirely from neutral phospholipids, such as distearoylphosphatidylcholine, and preferably ones which have been further stabilized with cholesterol or like-acting substances, for example in a molar ratio of distearoylphosphatidylcholine:cholesterol of about 2:1, respectively, have been found to be particularly suitable with regard to targeting efficiency when used to deliver anthracycline antineoplastic agents.

Detailed Description Text (2):
A mixture of chemically pure distearoyl phosphatidylcholine and cholesterol was dissolved in a 2:1 molar ratio in a chloroform/methanol solution. This solution was then dried to form a finely divided powder. The lipid powder was then hydrated in a buffer comprising 125 mM sucrose, 50 mM citric acid and 125 mM ethylenediamine at a pH of 7.5, at 65.degree. to 72.degree. C. for one hour. This dispersion was then homogenized in the modified Gaulin homogenizer (according to the method described in U.S. Pat. No. 4,753,788) at 10,000 psi. This procedure formed small unilamellar vesicles, which were then filtered through a 0.8 .mu.m AAWP Millipore filter membrane at 65.degree. C.

Detailed Description Text (8):
Liposomes were loaded with daunorubicin according to the method described in U.S. Pat. No. 4,946,683, the disclosure of which is incorporated herein by reference. A

dried lipid powder comprising 2:1 DSPC:cholesterol was added to a hydrating buffer comprising 125 mM sucrose and a 50 mM citric acid (buffer pH 2.2) at 50.degree. C. and held for 3 minutes. This dispersion of lipids was then homogenized in a modified Gaulin homogenizer, described in U.S. Pat. No. 4,946,683, at 10.2K psi to produce unilamellar vesicles having a diameter of from 40 to 90 nm Daunorubicin was loaded into these vesicles by first heating the vesicles in the hydrating buffer to 55.degree. C., adding 3 grams per liter daunorubicin hydrochloride, adjusting the pH of the external (continuous) phase to 6.28 with either sodium hydroxide or sodium bicarbonate, and incubating the dispersion at 55.degree. C. for 20 minutes.

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L11: Entry 46 of 58 File: USPT Jun 24, 1997

DOCUMENT-IDENTIFIER: US 5641508 A
TITLE: Method for delivering melanin to hair follicles

Detailed Description Text (54):
The lipid bilayer of the liposomes comprises phospholipids, preferably, phosphoglycerides. Exemplary liposome compositions include phosphatidylcholine (PC) liposomes, particularly egg PC (EPC) and dipalmitoyl PC (DPPC). Additional candidate liposome compositions are prepared according to the teachings of U.S. Pat. No. 4,394,488, the teachings of which are incorporated by reference, particularly the descriptions of liposomes comprising phosphotidylethanolamine (PE), phosphotidylserine (PS), sphingolipids, phosphotidylglycerol (PG), phosphatidic acid (PA), cholesterol, spingomyelin cardiolipin, various cationicphospholipids glycolipids, gangliosides, cerebrosides and the like, used either singularly or in combination.

Detailed Description Text (59):
Liposomes are preferably prepared using one or more phospolipids including (N-(1-(2,3-dioleolyoxy)propyl)-N,N,N-trimehtyl ammonium chloride) (DOTMA), dioleoylphosphatidylethanolamine (DOPE), dioleoylphosphatidylcholine (DOPC), phosphatidylethanolamine (PE), egg PC (EPC), phosphatidylcholine (PC), dipalmitoyl PC (DPPC), cholesterol and the like phospholipids. Phospholipids can be obtained from a variety of sources, including Avanti (Birmingham, Ala.), GIBCO BRL (Gaithersburg, Md.) and Aldrich (Milwaulkee, Wis.), or can be prepared from available materials, as is well known.

Detailed Description Text (64):
In one embodiment, the liposome composition of this invention contains one or more of the above cationic phospholipids. Preferably, a liposome composition of this invention comprises a formulation of phospholipids comprising a mixture of (a) one or more of the phospholipids PC, EPC, DOPC, DPPC, PE, DOPE, cholesterol and the like phospholipids, and (b) one or more of the cationic phospholipids D282, D378, D383, D3886, D3897, D3899 and the like. A particularly preferred liposome composition comprises a mixture of phospholipid (a) and cationic phospholipid (b) in a ratio of about 0.5 to 2.0 moles of phospholipid (a) to about 0.5 to 1.5 moles of phospholipid (b), and more preferably about 1.0-1.2 moles of phospholipid (a) to 0.8 moles of cationic phospholipid (b). A preferred phospholipid composition in this embodiment comprises a mixture of DOPC or DOPE with one or more of the above cationic phospholipids in a ratio of about 0.8 moles to about 1.0-1.2 moles.

Detailed Description Text (65):
In another embodiment, the invention comprises a liposome composition comprising one or more phospholipids selected from the group consisting of PC, EPC, DOPC, DPPC, PE, DOPE and cholesterol, combined with one or more phospholipids to form pH-sensitive liposomes. pH-sensitive liposomes are generally well known and their preparation has been described by Straubinger et al., FEBS Letts., 179:148-154 (1985). A preferred pH sensitive liposome comprises oleic acid (OA) and PE at a mole ratio of 3:7. OA is available from a variety of commercial sources, including Sigma (St. Louis, Mo.).

Detailed Description Text (183):

To that end, liposomes were prepared by well known freezing and thawing methods. About 20 mg of phospholipid in a ratio of 5:3:2 of phosphatidylcholine (PC): cholesterol (Chol): phosphatidylethanolamine (PE) was rotary evaporated with a vacuum drier from a chloroform solution for 1 hour to form a thin film on the walls of a 5 ml round-bottomed flask for about 1 hour. The dried film phospholipid was suspended in 2 ml phosphate buffered saline solution at a pH of about 7.4 (PBS) in a vortex mixer and then sonicated with a Branson probe-type sonicator fitted with a microtip at power level 3 for about 8 minutes. Then 200 ug of the plasmid pRHOHT2 was entrapped in a liposome by addition of the plasmid to the sonicated suspension, sonication of the admixture in a water bath for 2 minutes, followed by freezing and thawing three times to form nucleic acid-containing liposome composition.

Detailed Description Text (194):
Liposomes were prepared as described in Example 3b, except that the phospholipids comprised PC, PE and cholesterol in a ratio of 5:2:3, and the ratio of plasmid DNA to phospholipid was 200 ug DNA per 20 mg total phospholipid.

CLAIMS:

6. The method of claim 1 wherein said liposomes are comprised of one or more phospholipids selected from the group consisting of phosphatidycholine, egg phosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylethanolamine, dioleoylphosphatidylethanolamine and cholesterol.

7. The method of claim 6 wherein said liposomes are comprised of phosphatidylcholine:phosphatidylethanolamine:cholesterol in a ratio of 5:2:3.

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